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Quality of life by proxy and mortality in institutionalized older adults with dementia

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Aim: This study aimed at analyzing the effect of quality of life (QoL) on mortality in older adults with dementia living in long-term care facilities.

Methods: A prospective observational cohort study was carried out on 412 residents aged older than 60 years, diagnosed with dementia according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition. Besides assessment of QoL (EQ-5D index by proxy) and perceived health status (EQ-VAS), baseline measurements included severity of dementia (Clinical Dementia Rating Scale [CDR]), comorbidity (number of self-reported chronic conditions), disability evaluation (Barthel Index), cognitive state (*Mini Examen Cognoscitivo*, a validated and modified Spanish version of the Mini-Mental State Examination) and depression (Cornell Depression Scale for Dementia). Sociodemographic and clinical variables were analyzed as potential effect modifiers and confounders in the relationship between QoL and mortality using a multivariate logistic regression analysis.

Results: After an 18-month follow up, 138 residents had died. Adjusting for CDR and Barthel Index, the odds of mortality were multiplied by 0.25 (95% CI 0.09–0.70) and 0.79 (95% CI 0.26–2.42) for every unit of change in the EQ-5D index in the residents with Cornell score <6 and ≥6, respectively.

Conclusion: The present study suggests that the effect of QoL on mortality in institutionalized adults with dementia should take into account the presence or absence of depression. In addition, residents with a greater disability and more advanced dementia should be a target for interventions in rehabilitation care. **Geriatr Gerontol Int 2014; ••: ••–••.**

Keywords: dementia, long-term care settings, mortality, older adults, quality of life.

Introduction

Population aging is prompting a rapid increase in neurodegenerative disorders. It is estimated that 4.6 million new cases of dementia appear in the world every year.[1] The prevalence and incidence of this disorder points to an exponential increase from 60 years-of-age onwards, affecting up to 50% of those aged older than 85 years.[2] In Spain, as in the rest of the world, Alzheimer's disease (AD) is the leading cause of dementia, with a prevalence of 5.6% in those aged over 75 years.[3] On account of its magnitude, and also its impact on the health and quality of life (QoL) of those who suffer from it, dementia has a significant impact on caregivers of patients with dementia, the healthcare system and social services, posing a challenge for the organization and provision of care, especially at the end of life.[4]

The cognitive and functional impairment of AD and other dementias is the major determinant of institutionalization and death in older adults.[5] According to a study carried out in five European countries, between 50% and 92% of patients with dementia died in nursing homes, while home deaths ranged from 3% to 5% in most countries.[6]

Despite the rise in the institutionalization of older adults and of deaths in long-term care facilities, most published studies have focused their attention on the determinants of mortality in community-dwelling older

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adults.[7,8] Among these, QoL appears as a robust measure integrating physical and mental health. A lower QoL was an independent risk factor for mortality even after adjustment for other known risk factors in non-institutionalized older adults and in cancer patients.[9,10]

Similarly, factors linked to a worse QoL, such as depression and difficulty in carrying out activities of daily living (ADL), have been associated with increased mortality in institutionalized older adults.[11,12] The presence of depression was a predictor of mortality 12 months after admission in long-term care facilities,[12] and disability was a determinant of survival in nursing home residents, especially those with cognitive impairment,[11] suggesting a possible modifier or confounder role of these factors in the QoL–mortality relationship.

There have been few studies of the QoL–mortality relationship, and the role of potential modifying or confounding factors, in institutionalized older adults with dementia. The present study aimed to analyze this relationship in a cohort of institutionalized older adults with dementia. To this end, the effect of QoL on mortality was adjusted for possible modifying or confounding variables from a set of sociodemographic and clinical features.

Methods

Study population

A multicenter longitudinal cohort study was carried out among institutionalized older adults in 14 residential care homes in Spain. We studied a sample of 525 people aged 60 years and older diagnosed with dementia, according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision. Residents were recruited consecutively. QoL, and sociodemographic and clinical variables were collected by a survey, and after 18 months we obtained information on the outcome variable (living *vs* deceased). The residents or their legal representatives, in the case of severe dementia, authorized their participation the present study by signing an informed consent. This study was approved by the ethics committee of the Institute of Health Carlos III in Madrid, Spain.

Data collection and measures

QoL was the primary exposure variable, and it was measured by the EQ-5D index.[13] Because of the participants' characteristics in the present study (older adults with dementia), the EQ-5D and EQ-Visual Analog Scale (VAS) were completed by proxy (a relative or a professional caregiver). The EQ-5D index by proxy is a brief, easy to use, reliable and valid measure of QoL in older adults with cognitive impairment.[14,15] The scale takes values between –1 (worse QoL) and 1 (best QoL), and it includes a Visual Analog Scale (EQ-VAS), where respondents report their health status from 0 (the worst possible health status) to 100 (the best possible health status).

The sociodemographic variables analyzed were age, sex, spouse or partner (yes/no), living children (yes/no) and frequency of contact with relatives (<1 *vs* ≥1) per week. Clinical variables included severity of dementia (Clinical Dementia Rating Scale [CDR]),[16] functional level (Barthel Index),[17] comorbidity (adapted from the Cumulative Illness Rating Scale-Geriatrics [CIRS-G]),[18] cognitive state (*Mini Examen Cognoscitivo* [MEC], a modified and validated Spanish version of the Mini-Mental State Examination)[19] and depression (Cornell Depression Scale for Dementia).[20] Although the EQ-5D includes dimensions about depression and functional ability, we also included specific measures of these aspects, as they are important QoL determinants in dementia patients.[21]

CDR was categorized as mild/moderate versus severe, and the Barthel Index as moderate dependency (>40) and severe dependency (≤40). The comorbidity scale was categorized according to the sample median, seven diseases.[22] The Cornell Depression Scale for Dementia was categorized as without depression (<6) and with depression (≥6).[23]

Statistical analysis

The sample was analyzed for differences between the groups (living *vs* deceased) by means of independent sample *t*-test for quantitative variables and χ^2-test for categorical variables. The relationship between the sociodemographic and clinical variables and EQ-5D was also studied by means comparison, and Pearson's correlation for age, MEC and EQ-VAS.

The relationship between QoL and mortality was analyzed by logistic regression models. The potential modifying variables of the relationship between EQ-5D and mortality were assessed by constructing EQ-5D first-order interaction terms. These terms were evaluated according to statistical criteria with the likelihood ratio test in separate logistic regression models for each of them. A lack of interaction was assumed in any models containing terms with $P > 0.05$, and their variables were analyzed as potential confounders. Confusion was considered if the variation between the odds ratio (OR) of the logistic regression model with confounders and the odds ratio of the model without these variables was ≥10%. In the reference model, which included all the interaction terms and the confounding variables, we evaluated absence of collinearity, linearity between quantitative variable EQ-5D and the logit of mortality, and the presence of at least 10 cases of deaths per variable. Statistical analyses were carried out with IBM SPSS Statistics 19 (IBM Corporation, Armonk, NY, USA).

Results

Of the 525 residents surveyed, 412 (78.5%) were followed up for an average of 19.4 months (SD 1.8) until the end of the study. The reasons for loss were: in 17.1% (90) of residents, the outcome was unknown due to change in the company that managed the residential care homes, which no longer participated in the study; and in 4.3% (23), the residents moved to another non-participating residential care home. The mean EQ-5D index in the 412 cases in which follow-up information was obtained was 0.13 (SD = 0.38) and 0.04 (SD = 0.37) in which this information was not obtained ($P = 0.024$). The latter also had more severe dementia, higher comorbidity and higher depression ($P < 0.001$).

At the end of the study, the incidence of death was 33.5% (138). Compared with the group of living residents, the deceased had a lower mean in the EQ-5D index ($P < 0.001$), older age ($P < 0.001$) and worse scores on the Barthel Index ($P = 0.002$) at baseline (Table 1).

Comparison of EQ-5D means showed no significant differences by sex, spouse/partner, presence of living children and frequency of contact with relatives. Similarly, there was no association between EQ-5D and age, whereas moderate positive correlations of 0.42 and 0.59 ($P < 0.001$), respectively, were observed between EQ-5D and the MEC and EQ-VAS variables. Meanwhile, the mean EQ-5D difference in terms of clinical variables showed that residents with mild/moderate CDR on average scored 0.4 points higher on the EQ-5D index than residents with severe CDR ($P < 0.001$). Similarly, in residents with a Barthel Index >40 (moderate dependency), the mean EQ-5D was 0.5 points higher than in those with an index of ≤40 (severe dependency; $P < 0.001$). The EQ-5D mean differences in terms of comorbidity and depression were not significant.

Table 1 Quality of life, sociodemographic and clinical characteristics of residents according to outcome

Variable	Living mean ± SD *n* (%) (*n* = 274)	Deceased mean ± SD *n* (%) (*n* = 138)
Age (years)*	84.7 ± 6.5	87.5 ± 7.0
Sex		
Female	224 (81.8)	113 (81.9)
Male	50 (18.2)	25 (18.1)
Spouse/partner		
No	214 (78.1)	114 (83.8)
Yes	60 (21.9)	22 (16.2)
Living children		
No	87 (31.8)	40 (29.0)
Yes	187 (68.2)	98 (71.0)
Contact with family		
≥Once a week	190 (70.4)	98 (72.6)
<Once a week	80 (29.6)	37 (27.4)
CDR (severity of dementia)		
Mild/moderate	121 (44.2)	54 (39.1)
Severe	153 (55.8)	84 (60.9)
Barthel Index (functional level)*		
>40 (moderate dependency)	112 (42.1)	35 (26.1)
≤40 (severe dependency)	154 (57.9)	99 (73.9)
Comorbidity (no. chronic problems)		
≤7	162 (59.6)	71 (51.8)
>7	110 (40.4)	66 (48.2)
MEC	13 ± 8.5	12.7 ± 7.6
Cornell scale (depression)		
<6 (without depression)	160 (61.5)	67 (56.3)
≥6 (with depression)	100 (38.5)	52 (43.7)
EQ-5D*	0.18 ± 0.38	0.04 ± 0.37
EQ-VAS	54.7 ± 20.4	48.8 ± 23.7

*$P < 0.05$. CDR, Clinical Dementia Scale; EQ-VAS, EQ-Visual Analog Scale; MEC, *Mini Examen Cognoscitivo* (Spanish version of the Mini-Mental State Examination [normal range ≥24]).

Effect of the quality of life on mortality

As a result of analysis of potential confounding and modifying factors in the relationship between EQ-5D and mortality (Table 2), the reference regression model included the interaction term Cornell × EQ-5D (Fig. 1), and confounding variables of CDR and Barthel Index.

After comparison of the reference model with the different reduced models resulting from eliminating each one of the confounding factors, in residents with Cornell Depression Scale <6 (without depression), the non-inclusion of the Barthel Index and CDR variables produced changes of 12% and 20% in the EQ-5D's effect on mortality, respectively. The adjusted effect of EQ-5D on mortality in the reduced model without the CDR variable (OR 0.28, 95% CI 0.10–0.76) was less than its effect in the reference model (OR 0.25, 95% CI 0.09–0.70). In contrast, the effect of the EQ-5D on mortality in the model without the Barthel Index (OR 0.20, 95% CI 0.08–0.49) was higher than in the reference model (Table 3).

In residents with the Cornell Depression Scale ≥6 (with depression), the non-inclusion of the CDR variables and Barthel Index produced changes of 9.0% and 16.5% between the adjusted and unadjusted effect of the EQ-5D on mortality, respectively. The non-inclusion of the CDR variable reduced the effect of the EQ-5D on mortality: in the reference model OR 0.79 (95% CI 0.26–2.42) versus 0.86 (95% CI 0.28–2.60) in the reduced model. In contrast, non-inclusion of the

Table 2 Analysis of potential modifying or confounding variables in the relationship between quality of life and mortality

Variable	Interaction test *P*-value (Likelihood ratio test)	Confounding analysis OR (95% CI)†	Change‡ (%)
Age	0.880	0.37 (0.21–0.66)	5.4
Sex	0.432	0.35 (0.19–0.62)	0
Spouse/partner	0.291	0.36 (0.20–0.64)	2.8
Living children	0.941	0.35 (0.20–0.62)	0
Contact with family	0.857	0.37 (0.21–0.65)	5.4
CDR (severity of dementia)	0.113	0.31 (0.16–0.59)	**12.9**
Barthel Index (functional level)	0.595	0.41 (0.19–0.88)	**14.6**
Comorbidity (no. chronic problems)	0.091	0.36 (0.20–0.64)	2.8
MEC	0.943	0.53 (0.25–1.15)	7.5
Cornell scale (depression)	**0.021**		
EQ-VAS	0.063	0.42 (0.21–0.87)	9.5

In bold *P*-value <5% in the interaction test and change ≥10% in the odds ration (OR). †OR of the regression model with the confounding variable. ‡Variation between the OR of the regression model with the confounding variable and the OR of the model without this variable. CDR, Clinical Dementia Scale; EQ-VAS, EQ-Visual Analog Scale; MEC, *Mini Examen Cognoscitivo* (Spanish version of the Mini-Mental State Examination).

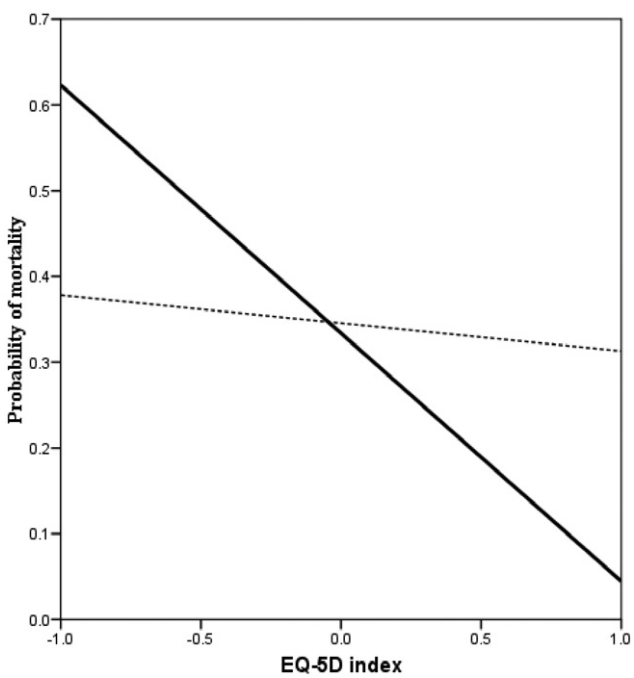

Figure 1 Interaction effect between EQ-5D index and Cornell Depression Scale on mortality. Straight line: effect of EQ-5D on mortality in residents without depression. Dashed line: effect of EQ-5D on mortality in residents with depression.

Barthel index increased the effect of the EQ-5D on mortality compared with the reference model (OR 0.66, 95% CI 0.25–1.77), but these associations were not significant (Table 3).

Given the observed changes in the EQ-5D effect on mortality in different reduced models, the CDR variables and Barthel Index were considered confounders of this relationship. Thus, after adjusting for the effect of CDR and Barthel Index, in residents with Cornell scale <6, a one unit increase in the EQ-5D index multiplied the mortality odds by 0.25 (95% CI 0.09–0.70), whereas in residents with a score of ≥6 on this scale, the mortality odds were multiplied by 0.79 (95% CI 0.26–2.42), without this effect being significant (Table 3).

Discussion

The present study aimed to analyze the relationship between QoL and mortality in institutionalized older adults with dementia, and the possible modifying or confounding role of a number of factors in this relationship. It was observed that the effect of QoL on mortality in residents with dementia varied in terms of the presence or absence of depression, the effect being higher in the absence thereof. For residents without depression, the risk of death was 75% lower per unit change in the EQ-5D index, whereas in residents with depression, the risk of death was 21% lower and not statistically significant. Meanwhile, both in residents with and without depression, the severity of dementia and functional level were confounders of this relationship in different ways.

The observed relationship between QoL and mortality, and the role of certain factors in the relationship, is a consistent finding in previous studies.[10,24] Bilotta *et al.* observed that low QoL multiplied the mortality odds by 4.23 (1.06–16.81) in community-dwelling older adults

Table 3 Final (reference model) and reduced models of adjusted effect of EQ-5D index on mortality

Model	Cornell Scale <6 OR (95% CI)	*P*	Cornell Scale ≥6 OR (95% CI)	*P*
Reference model†	0.25 (0.09–0.70)	0.008	0.79 (0.26–2.42)	0.673
Reduced model 1‡	0.28 (0.10–0.76)	0.013	0.86 (0.28–2.60)	0.784
Reduced model 2§	0.20 (0.08–0.49)	<0.001	0.66 (0.25–1.77)	0.409

†Adjusted odds ratio (OR) by Cornell × EQ-5D, Clinical Dementia Scale and Barthel Index. ‡Adjusted OR by Cornell × EQ-5D and Barthel Index (without Clinical Dementia Scale). §Adjusted OR by Cornell × EQ-5D and Clinical Dementia Scale (without Barthel Index).

after controlling, among other factors, for depression, dementia severity and difficulty carrying out ADL;[13] whereas Cavrini *et al*. found that for the increase of each EQ-5D index unit, the hazard ratio for mortality at 12 and 24 months decreased by 69% and 58%, respectively, in older adults.[25]

In contrast to most of the literature that supports a positive association between depression and mortality in older adults, the present study found, in the crude analysis, no significant differences between residents with and without depression in the incidence of mortality.[7,26,27] The lack of association might be explained by varying methods for assessing depression.[28] In this regard, a study on dementia depression in nursing home residents noted that a cut-off score of >5 on the Cornell scale showed the highest sensitivity (100%), but low specificity, just 43%,[20] which suggests that this scale might be better used for ruling out rather than for ruling in depression. Thus, some of the patients classified as having depression might be false positives who do not really show characteristics of a higher mortality risk.

Dementia severity and functional level met the key criteria for being confounding factors. From an epidemiological perspective, there is little evidence to consider that the severity of dementia or functional level are intermediate factors in the QoL-mortality etiopathogenic pathway.

The decrease in the protective effect of QoL on mortality, after adjusting for functional level, can be explained by the higher mortality in severely disabled residents observed in the present study, in addition to the large proportion of residents with poor functional level in the sample (63.3%). Besides, both functional level and dementia severity have been described as independent predictors of mortality in institutionalized older adults.[29–32]

The literature supports the conceptualization that QoL in long-term care settings is a process influenced by many variables interacting with one another, in which cognitive, emotional and functional capacity variables are interrelated.[33,34] In the present study, the higher adjusted effect of the QoL on mortality in adults without depression might be explained by a favorable condition secondary to the absence, at least partially, of this emotional factor. The lack of depression might improve the functional level performance, which in turn would positively influence QoL.[33]

The present study presented some limitations. First, because it was a consecutive sample, generalizations should be made with caution. However, observed relationships between variables were consistent with findings from other studies. In addition, the intensity of QoL's protective effect on mortality might be underestimated if one considers that the cases lost in the present study had a worse QoL, greater depression and comorbidity, and more severe dementia at baseline than residents with tracking data. This is a common limitation to most follow-up studies, and an effort was made to characterize in which way the groups differed.

It is expected that the period affects the mortality, with time-dependent higher rates.[25,31] As a previous study reported a median survival of nursing home residents with advanced dementia of 16 months,[31] we used a higher follow-up time, 18 months. However, we did not have information about the exact period of time between recruitment and event, collecting the outcome variable as living or deceased. Thus, in order to know survival time and mortality rates, survival analysis should be carried out in future studies about QoL and mortality in institutionalized older adults. As for the instrument used, although the EQ-5D is a generic QoL questionnaire that is not specific for dementia patients, there is sufficient evidence of its validity in older people with and without cognitive impairment.[14,18] Considering the subjective nature of the QoL, it is generally agreed that any assessment should be based on individual perception. The use of proxies to measure QoL has inherent obstacles, such as a low association between the proxy and patient, which depends on the nature of the relationship between the patient and proxy, the level of caregiver burden and the level of patient's cognitive impairment.[35] However, the EQ-5D by proxy has been successfully used when patients are too severely impaired to complete the ratings themselves.[14]

In conclusion, the findings suggest that the assessment of QoL in institutionalized adults with dementia should take into account the presence or absence of depression. Furthermore, improvements in the QoL of institutionalized older adults must go hand-in-hand with disability rehabilitation interventions, as well as efforts to slow down the progression of dementia, so as to enhance the protective effect of QoL on mortality.

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Disclosure statement

The authors declare no conflict of interest.

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